

Curative effect of the recent photofrin photodynamic adjuvant treatment on young patients with advanced colorectal cancer

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Abstract. Advanced colorectal cancer has a high mortality rate and conventional treatments have poor therapeutic effects. The aim of the present study was to analyze the recent curative effect and adverse reaction of photofrin photodynamic adjuvant treatment on young patients with advanced colorectal cancer. A total of 23 patients with advanced colorectal cancer who had accepted semiconductor laser photodynamic adjuvant treatment were selected as the observation group. In addition, 30 patients who had accepted concurrent radiotherapy and chemotherapy during the same period served as the control group. The observation group received photofrin (2 mg/kg) intravenously in 100 ml of 5% glucose, followed by the introduction of the endoscopic optical fiber to deliver laser radiation with an intensity of 630 nm wavelength pulse power. After 2 days, necrotic tissues were removed and irradiation of the original or new tumor lesions was performed and necrotic tissues were removed. The total effective rate and survival time was higher and the length of hospital stay was shorter in the observation group in comparison with the control group. The differences were statistically significant ($P < 0.05$). The number of patients in the control and observation groups with symptoms of hemochezia, change in bowel habit, intestinal stimulation and incomplete intestinal obstruction were reduced. Additionally, the reduced ratio of the observation group was significantly increased in comparison with the control group ($P < 0.05$). The adverse reaction rate of the observation group was lower than that of the control group and this difference was also statistically significant ($P < 0.05$). In conclusion, use of photodynamic treatment for young patients with advanced colorectal cancer can effectively improve the clinical symptoms and reduce complications.

Introduction

The incidence and mortality rates of advanced colorectal cancer have been on the increase in recent years. Data presented at the 8th Shanghai International Settlement rectal cancer forum in 2012 demonstrated that the incidence of colorectal cancer is the highest in western developed countries with regard to malignancies and ranks fourth in China. The mortality rate ranks second in developed countries and sixth in China (1). The pathogenesis of the disease is associated with genetic and long-term chronic intestinal inflammation (2). Early clinical symptoms are atypical and 40-50% patients have been diagnosed with metastasis due to a lack of specific screening tools (3). The degree of malignancy is higher especially for young patients (4). Conventional treatments such as surgical resection, radiotherapy and chemotherapy have poor therapeutic effects and considerable side effects (5). Microwave and high power laser treatments can increase severe complications including intestinal bleeding, esophageal mediastinal fistula or esophagotracheal fistula (6,7). As a means of local tumor ablation, photodynamic therapy (PDT) has been developing rapidly in recent years. PDT has a slight effect on normal tissues, but can kill tumor cells selectively and repeated treatment improves the therapeutic effect (8). PDT is beneficial in the treatment of colorectal cancer, it does not cause cicatricial stenosis. In addition, it can significantly improve the quality of life of patients with cancer and extend their life span (9,10). PDT has been widely applied in the treatment of throat, bladder, lung, esophageal, and gastric cancer (11).

In the present study, semiconductor laser PDT was used to treat 23 young patients with advanced colorectal cancer and its importance for the clinical treatment of advanced colorectal cancer was assessed.

Patients and methods

Patients and control. Twenty-three patients with advanced colorectal cancer who had accepted semiconductor laser PDT were chosen between September, 2010 and February, 2014 in The First People's Hospital of Xuzhou as the observation group. The patients did not undergo surgery, could not be relieved of the complete or incomplete obstruction and experienced relapse after accepting radiotherapy, chemotherapy and surgical resection. Of the 23 patients, 16 were men and

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Table I. Clinical efficacy of the treatment.

Groups	Patients	CR	PR	MR	NR	Total effective rate	Survival time (months)	Length of hospital stay
Control	30	2	5	5	18	40	3.01±1.12	19.72±5.21
Observation	23	2	6	8	7	69.57	6.23±1.65	13.47±4.46
t						2.341	3.846	2.212
P-value						0.035	0.013	0.036

CR, complete response; PR, partial response; MR, mild response; NR, no response.

Table II. PDT treatment relieved the clinical symptoms.

Groups	Patients	Before treatment			After treatment		
		Hematochezia	Bowel habits and intestinal stimulation	Incomplete intestinal obstruction	Hematochezia	Bowel habits and intestinal stimulation	Incomplete intestinal obstruction
Control	30	9	17	4	7	12	3
Observation	23	6	13	4	3	7	2

PDT, photodynamic therapy.

Table III. Adverse reaction rate reduced in PDT treatment.

Groups	Patients	Intestinal, rectovesical fistula or rectovaginal fistula	Photosensitive dermatitis	Lower gastrointestinal hemorrhage	Myelosuppression, liver and kidney toxicity	Others
Control	30	5	3	4	2	1
Observation	23	2	1	3	0	

PDT, photodynamic therapy.

7 were women, with an age range of 23-58 years with a median age of 41.9 years. Of the 23 patients, 21 had rectal cancer and 2 had sigmoid carcinoma. Advanced colorectal cancer in the 23 patients was confirmed pathologically, 10 patients were in Dukes C stage and 13 patients were in D stage. Seven patients had liver metastasis and 16 patients were out of control after accepting to undergo chemotherapy. Four patients had tumor recurrence after surgical resection and three patients had tumor recurrence after radiotherapy. Hematochezia was observed in 6 patients, a change in bowel habit and intestinal stimulation was observed in 13 patients, and 4 patients exhibited incomplete intestinal obstruction. Thirty patients who accepted concurrent radiotherapy and chemotherapy served as the controls. Of the 30 patients, 21 were men and 9 were women, with an age range of 27-56 years, and a median age of 41.9 years.

The study was approved by the ethics committee of The First People's Hospital of Xuzhou. Written informed consent was provided by the patients.

PDT. Laser therapy was performed using Diomed 630 (British Laser Instrument Co., Ltd., Diomed, Cambridge, UK) with an

output of 630 nm wavelength pulse power. The optical fibers included were column-shaped and flat cut fibers. The length of the terminal of the column-shaped fiber was 2-5 cm and the photosensitizer was photofrin (Canadian Pharmaceutical Co., Ltd., Québec, Canada).

Photofrin at a final concentration of 2 mg/kg was administered to the patients intravenously in 100 ml of 5% glucose. After 48 h, laser irradiation at 630 nm was delivered through a flat cut optical fiber. For different lesion ranges, different lengths of column-shaped fibers were used. The irradiation dose of different types set in the machine was in accordance with differences of the tumor length in the cavity. Normally, 1-3 segments were irradiated each time and the irradiating time was ~12 min, with an energy density of 200 J/cm². Each segment was interlinked when treated, at least exceeding 0.5 cm of the tumor boundary, leading to the illumination range completely covering the tumor area. The necrotic tissues were removed endoscopically after 2 days and repeated irradiations were performed at the original tumor and new tumor sites to improve the therapeutic effect. The patients underwent enteroscopic examination after one month to monitor the therapeutic

effect of the treatment. It was identified that 5 patients used intestinal stent after laser radiation.

Curative effect. The general standards to classify colon cancer in the present study were: i) complete response (CR), where the tumor completely disappeared, tissue histopathology was negative and this condition lasted ≥ 1 month; ii) partial response (PR), where tumor maximum diameter and vertical diameter or the tumor height narrowed $>50\%$ and this condition lasted ≥ 1 month; iii) mild response, where the tumor narrowed $<50\%$ and this condition lasted ≥ 1 month; iv) no response, no change or enlargement of the tumor.

Statistical analysis. The SPSS 17.0 software (SPSS, Inc., Chicago, IL, USA) was used to analyze the results. Data were presented as mean \pm standard deviation. Comparisons between groups was performed by t-test and Chi-square test. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Clinical efficacy of the PDT treatment. The patient age, gender and stages of cancer were not significantly different between patients in the observation and control groups ($P > 0.05$). The total effective rate of the observation group was significantly higher when compared with that of the control group. An increased survival time and decreased length of hospital stay was also identified in patients of the observation group in comparison with those of the control group (Table I).

Clinical symptoms relieved in patients who had received PDT. The number of patients exhibiting symptoms including hematochezia, change in bowel habits, intestinal stimulation and incomplete intestinal obstruction were distributed similarly prior to treatment in the two groups. However, following PDT treatment, the number of patients exhibiting these symptoms became reduced in the observation group. Conventional treatments such as radiotherapy and chemotherapy did not reduce the number of patients with these symptoms, as is evident in the control group. Additionally, the reduced ratio in the observation group was significantly higher than that of the control group ($\chi^2 = 2.094$, $P = 0.041$; Table II).

Adverse reaction rate reduced in PDT treatment. The adverse reaction rate in the observation group was significantly reduced compared to that of the control group ($\chi^2 = 2.997$, $P = 0.031$; Table III).

Discussion

PDT comprises a photosensitizer, laser and dioxygen, and each substance is harmless to cells (12). The rapid development of the photosensitizer and laser irradiation systems has led to PDT gradually becoming a new method used in the treatment of various types of tumor (13). The biological mechanism of PDT has been fully understood. The basic principle is the photochemistry principle of the photodynamic laser, which utilizes a laser of specific wavelength to activate the photosensitizer remaining in the tumor tissues. Thus, the photosensitizer operates with oxygen in tumor tissues,

producing robust radicals from singlet oxygen. Consequently, colon cancer cells are attacked by oxidation, subsequently killing tumor cells (14,15).

PDT has gradually become an anticancer strategy employed in the treatment of colorectal cancer (16). Compared with traditional anticancer strategies such as surgery, radiotherapy and chemotherapy, PDT has numerous inherent advantages including accurately positioning target tumor tissues, relatively non-invasive treatment, non-requirement of repeated drug administration, relative ease of operation, fewer side-effects, little trauma, low toxicity, wide range of applications, protecting appearance and important organ functions, less irradiation to the blind region, relatively steady curative effect, selective damage to tumor tissues and suitability for colon cancer patients of all ages and stages (17-19).

Previous studies focusing on progressive stage colon cancer have demonstrated that the PR rate of patients is 44% and the CR rate is 35% (20,21). The total effective rate of PDT for patients with advanced colon cancer to control bleeding, relieve pain and intestinal obstruction reached 70% (22,23). In this study, the total effective rate of the observation group was significantly higher than that of the control group. The former's survival time was also significantly higher and the length of hospital stay was significantly reduced. Furthermore, it was identified that the symptoms of patients in the observation group with hematochezia, change in bowel habits, intestinal stimulation and incomplete intestinal obstruction were alleviated and the adverse reaction rate was markedly decreased. A minor adverse reaction was primarily skin photosensitivity following laser irradiation. The curative effect of the photosensitizer with laser irradiation treatment was therefore more beneficial than conventional treatments. Thus, photofrin photodynamic treatment on young patients with advanced colorectal cancer can be used as an adjuvant treatment option and has relatively great clinical value for promotion.

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